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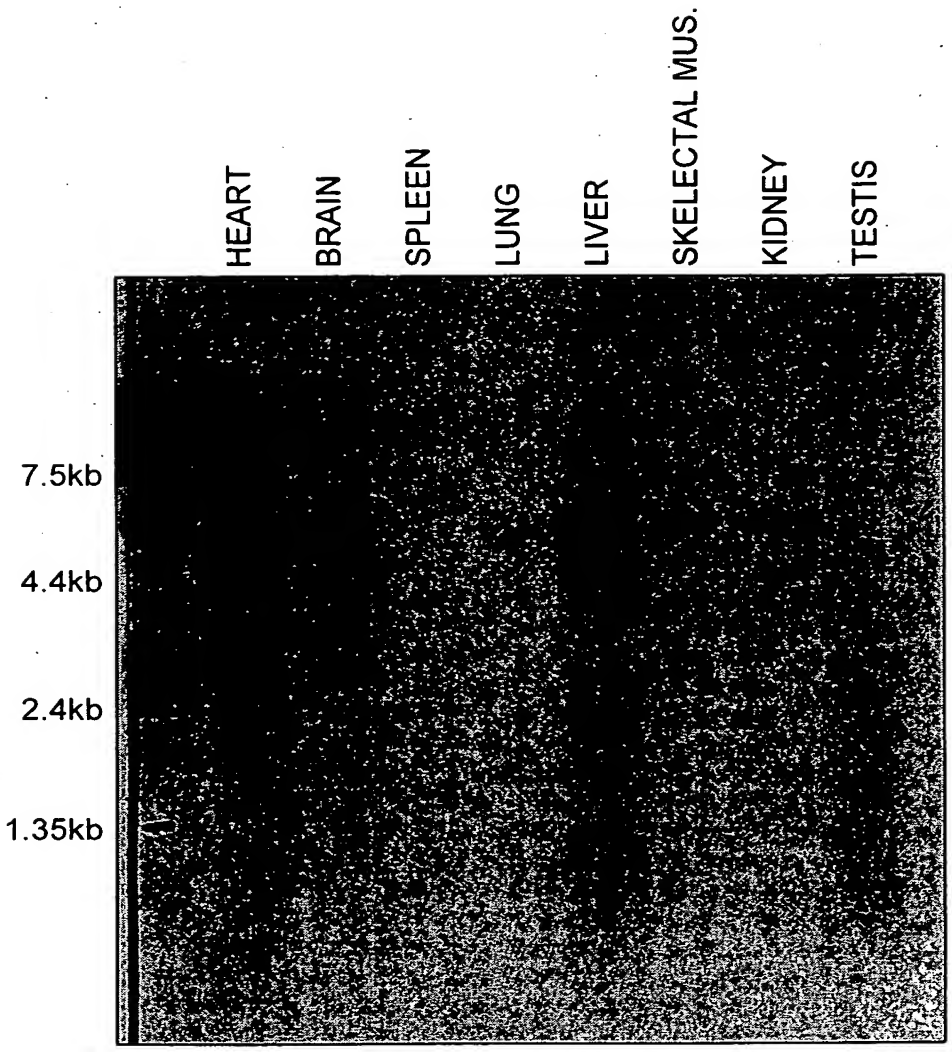

FIG. 1

MURINE MTN BLOT PROBED WITH
^{32}P-LABELLED MURINE PDE_XIV

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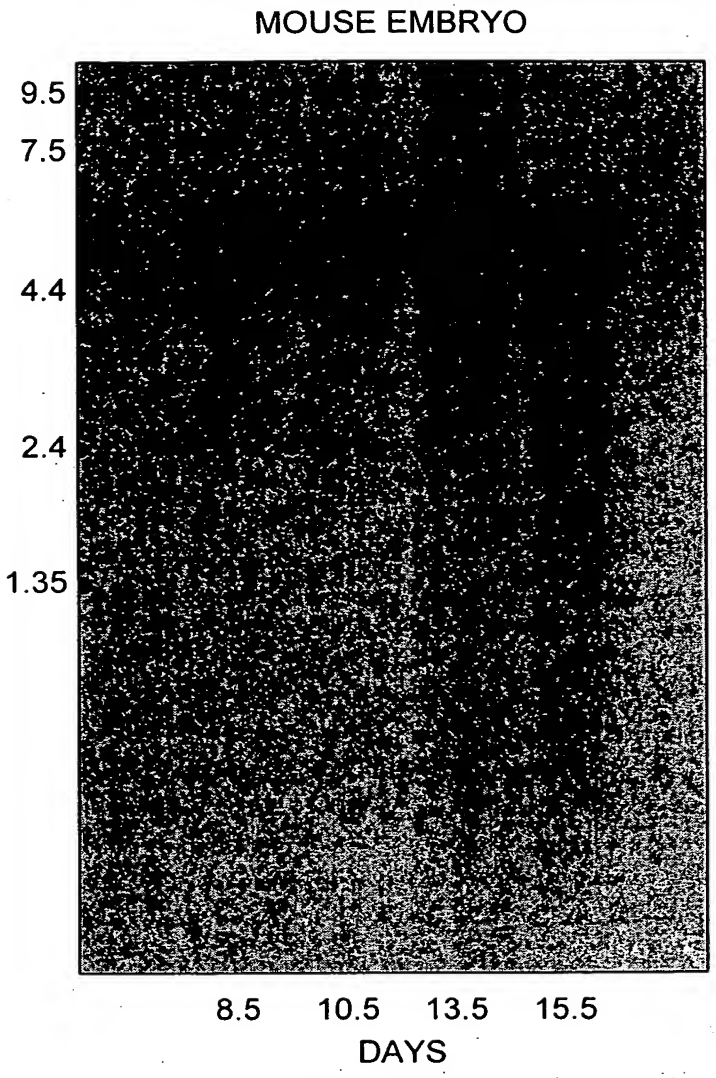

FIG. 2

MURINE EMBRYO MTN BLOT PROBED WITH 32P-LABELLED MURINE PDE_XIV

	1	2	3	4	5	6	7	8
A	WHOLE BRAIN	AMYG-DALA	CAUDATE NUCLEUS	CERE-BELLUM	CEREBAL CORTEX	FRONTAL LOBE	HIPPO-CAMPUS	MEDULLA OBLON-GATA
B	OCCIP-ITAL LOBE	PUTAMEN	SUBST-ANTIAL NIGRA	TEMP-ORAL LOBE	THALA-MUS	NUCLEUS ACCUM-BEUS	SPINAL CORD	
C	HEART	SORTA	SKELETAL MUSCLE	COLON	BLADDER	UTERUS	PROST-ATE	STOMACH
D	TESTIS	OVARY	PANC-REAS	PITUIT-ARY GLAND	ADRENAL GLAND	THYROID GLAND	SALIVARY GLAND	MAMM-ARY GLAND
E	KIDNEY	LIVER	SMALL INTE-STINE	SPLEEN	THYMUS	PERIPH-ERAL LEUKO-CYTE	LYMPH NODE	BONE MARROW
F	APPEN-DIX	LUNG	TRACHEA	PLACEN -TA				
G	FETAL BRAIN	FETAL HEART	FETAL KIDNEY	FETAL LIVER	FETAL SPLEEN	FETAL THYMUS	FETAL LUNG	
H	YEAST TOTAL RNA 100ng	YEAST tRNA 100ng	E. COLI rRNA 100ng	E. COLI DNA 100ng	POLY r(A) 100ng	HUMAN C_0t1 DNA 100ng	HUMAN DNA 100ng	HUMAN DNA 500ng

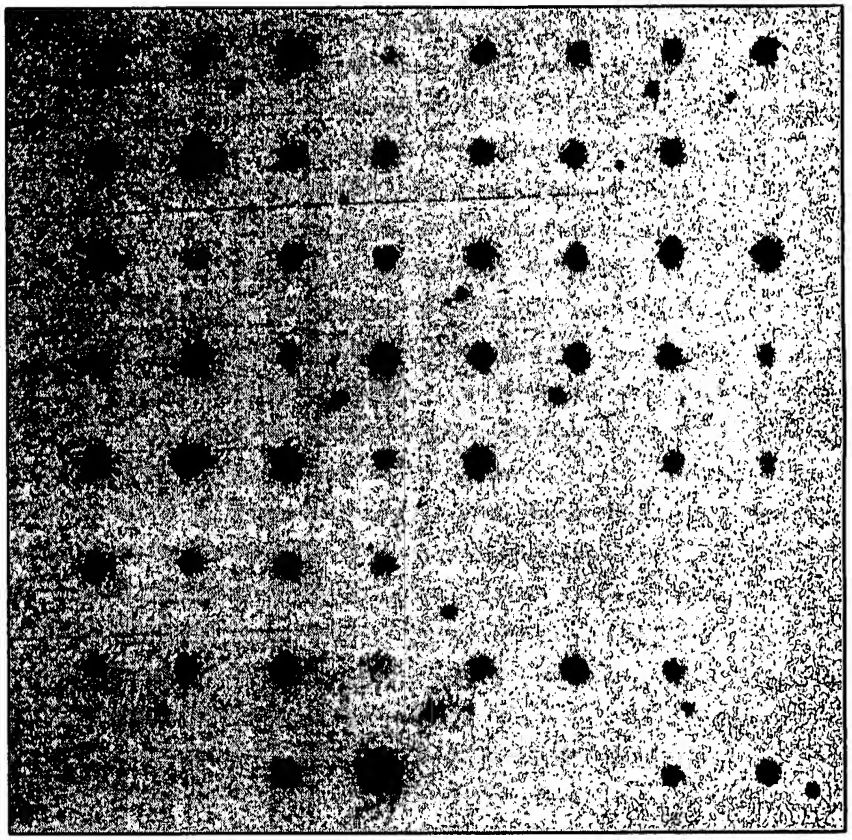

FIG. 3

HUMAN RNA MASTER BLOT PROBED WITH
^{32}P-LABELLED HUMAN PDE_XIV

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FIG. 4

Alignment of the Murine and Human PDE_XIV nucleotide sequence

```
New sequence is PDE_XIV

Pileup: Genetics Computer Group.
   MSF: 3134  Type: N    Check:  5422   ..

 Name: mpdea_ oo  Len: 3134  Check:  5084  Weight:  0.001
 Name: hspdea_ oo  Len: 3134  Check:  338  Weight:  0.100

new mpde_        1 AGGTACGCCT GCAGGTACCG GTCCGGAATT CCCGGGTCGA CCCACGCGTC
new hspde_         .......... .......... .......... .......... ..........

new mpde_       51 CGGCCAGCCT CCCAGGCCGG CTGCCTGCTC ACCCAGCCAG TCGCTAGCTC
new hspde_       1 .......... .......... .......... .......... .CGGAAT.TC

mpdea_         101 TGGGCACTGC AGCAGGCTCG GCTCTGTCCC AGCGCTCGCT TGCTTGCTCG
hspde_           9 GATGCACTGC AGCAGGCTCG GCTCTGTCCC AGC....A.. ..........

mpdea_         151 CTCGCTCGGC TGGGAGAAAA GTGGTGTC.C TCGCCCAG.. AGAGCCTCTC
hspde_          43 ....CTTGTC TGGGAGAAAA GTGGTGTTAC TCACCCAGGG AGAGTCTCTC

mpdea_         198 TCTC..CCTT CCTTCTTTCT CGAGCTCTCT GAGTCCTTTG GCGTTTCTTT
hspde_          89 TTTCTACCTT CCTTCTTTCT CGATCTCCTT GTGTGCTTTT GTGTTTCTTT

mpdea_         246 CTTTCTTTCC TTTTTTTTTT TTTTTTAATA TTTTCTTTTT CTTTCTATAA
hspde_         139 ATTTCTTTTC CTTTTTTTTC TT........ TTTTTTTTTT GTTACT....

mpde_          296 AACTTGCATA ATTATACTGC TAATCCTGGA TGAGGTTGCT GGATTCTGCA
hspde_         177 ........TA ATTATATTCC TAATCCTGGA TGAAGTTGCT GGATTCTGCA

mpde_          346 GCACAAATCT TCATGAACAA GCCGCACCGC TCAGAGATTT CACAGCATTC
hspde_         219 GCACAAGTCT TCATGAACAA GCAGCACCGC TCAGAGATTT CACGGCATTC

                                                  start codon
mpde_          396 AAAGGTCACA GAACTGCCAC TATGGTTAAA TGTCTTGTTT AATGGTTGAG
hspde_         269 AAAGGTCACA GAACTGCCAC TATGGTTAAA TGTCTTGTTT AATGGTTGAG

mpdea_         446 AGGTGTGGCG AAGTCTTGTT TGAGAGCCCT GAACAGAGTG TCAAATGTGT
hspde_         319 AGGTGTGGCG AAATCTTGTT TGAGAACCCC GATCAGAATG CCAAATGTGT

mpde_          496 TTGCATGCTA GGAGATGTAC GACTAAGGGG TCAGACGGGG GTTCCTGCCG
hspde_         369 TTGCATGCTG GGAGATATAC GACTAAGGGG TCAGACGGGG GTTCGTGCTG

mpde_          546 AACGCCGTGG CTCCTACCCA TTCATTGACT TCCGTCTACT TAACAATACA
hspde_         419 AACGCCGTGG CTCCTACCCA TTCATTGACT TCCGCCTACT TAACAGTACA

mpde_          596 ACACACTCAG GGGAAATTGG CACCAAGAAA AAGGTGAAAC GACTGTTAAG
hspde_         469 ACATACTCAG GGGAGATTGG CACCAAGAAA AAGGTGAAAA GACTATTAAG

mpde_          646 TTTCCAAAGA TACTTCCATG CATCTAGGCT TCTCCGGGGG ATTATACCGC
hspde_         519 CTTTCAAAGA TACTTCCATG CATCAAGGCT GCTTCGTGGA ATTATACCAC

mpde_          696 AGGCCCCTCT CCACCTGCTG GATGAAGACT ACCTTGGACA AGCAAGGCAC
hspde_         569 AAGCCCCTCT GCACCTGCTG GATGAAGACT ACCTTGGACA AGCAAGGCAT

mpde_          746 ATGCTCTCCA AAGTTGGAAC GTGGGACTTT GACATTTTCT TGTTTGATCG
hspde_         619 ATGCTCTCCA AAGTGGGAAT GTGGGATTTT GACATTTTCT TGTTTGATCG
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FIG. 4CONT'D

```
mpde_      796 CTTGACAAAT GGGAACAGTC TGGTAACTCT GTTGTGTCAC CTCTTCAACT
hspde_     669 CTTGACAAAT GGAAACAGCC TGGTAACACT GTTGTGCCAC CTCTTCAATA

mpde_      846 CCCATGGGCT CATCCACCAT TTCAAGCTCG ATATGGTGAC CTTGCACAGG
hspde_     719 CCCATGGACT CATTCACCAT TTCAAGTTAG ATATGGTGAC CTTACACCGA

mpde_      896 TTTCTGGTTA TGGTTCAGGA AGATTACCAC GGTCACAACC CATACCACAA
hspde_     769 TTTTTAGTCA TGGTTCAAGA AGATTACCAC AGCCAAAACC CGTATCACAA

mpde_      946 TGCTGTTCAC GCAGCCGACG TCACCCAGGC CATGCACTGT TACCTGAAGG
hspde_     819 TGCTGTTCAC GCAGCCGACG TCACCCAGGC CATGCACTGC TACCTGAAAG

mpde_      996 AGCCAAAGTT GGCAAGCTTC CTCACACCTC TGGACATCAT GCTTGGACTA
hspde_     869 AGCCAAAGCT TGCCAGCTTC CTCACGCCTC TGGACATCAT GCTTGGACTG

mpde_     1046 CTGGCTGCAG CAGCTCATGA CGTGGACCAC CCAGGGGTCA ACCAGCCATT
hspde_     919 CTGGCTGCAG CAGCACACGA TGTGGACCAC CCAGGGGTGA ACCAGCCATT

mpde_     1096 TTTGATCAAA ACTAACCACC ATCTTGCCAA CCTGTATCAG AATATGTCTG
hspde_     969 TTTGATAAAA ACTAACCACC ATCTTGCAAA CCTATATCAG AATATGTCTG

mpde_     1146 TACTGGAGAA TCACCACTGG CGATCTACAA TTGGCATGCT TCGAGAATCA
hspde_    1019 TGCTGGAGAA TCATCACTGG CGATCTACAA TTGGCATGCT TCGAGAATCA

mpde_     1196 CGGCTCCTGG CTCACTTGCC AAAGGAAATG ACACAGG... .....ATATC
hspde_    1069 AGGCTTCTTG CTCATTTGCC AAAGGAAATG ACGTAAGTGC TGCCGAGATG
                                                 stop codon

mpde_     1238 GAACA..... ....GCA... ......GCTG GGCTCCCTCA TCTTGGCCAC
hspde_    1119 AAACATACTG ATGTGCATGC AGTAAAGATA AGCCACTTTC TCTAGGGCA.

mpde_     1270 GGATATCAAC AGACAGAATG AGTTTCTGA. ......CCCG CTTAAAAGCT
hspde_    1168 GGCTTGGGAC CTTTTGCGTG AATGGCAGAG AGCCCCCCGG CTGTACTTCC

mpde_     1313 CACCTCCACA ATAAAGATT. TGAGAC.... ..TGGAGAAT GT.ACAGGA.
hspde_    1218 TGCCTGCACT GAGCTGTCTA TCAGAGGAGA TTTGGTGTCA GTTACAGCAA

mpde_     1354 ..CAGACACT TTATGCT.TC AGATCGCCTT GAAGTGTGCT GACATTTGCA
hspde_    1268 CCCAGAAACC AAAATCTCTC TGTGTGCTTT GAAAGGGCCT TGCAGAGTCA

mpde_     1401 AT..CCTT.. GTC.GTATCT GGGAGATGAG CAAGCAGT.. GGAGTGAAAG
hspde_    1318 ATGACCTACA GTCAGGAAAA GGGATAATAA ACAGCTCTCA GTTTTCACAC

mpde_     1444 GGT..... CTGTGAGGAA TTCTACAGAC AAGGTGACCT TGAAC..AG.
hspde_    1368 GCTTCAGTAT CAGTGCTCAA CTTTGCCAAA TTCCCGACCT TTAGTTTAGC

mpde_     1484 AAGTTTGAAC TGGAAATCAG .TCCTCTTTG TAATCAAC.A GAAAGATTCA
hspde_    1418 AAAATTGTCC TTCCATGTAG CTCCAAATAG TAAATATTTA TCAAGAAGGA

mpde_     1532 ATCCCTAGCA TACAAA...T TGGTTTCATG ACT.TACATC GTGGAGCCGC
hspde_    1468 A.CCCAGGCA TTCTAAAGCT AGAGTTCAAA AAAGTATATT TTGTAATTGC

mpde_     1578 TGTTCCGGG. ...AGTGG.. GCCCGGTTTA CTGGG..AAC AGCACCCTGT
hspde_    1517 TAGTCTCAGC AAAAATAGAA GTCAGAAATT CTTTTCTAAA ATGTCTTTTG

mpde_     1620 CGGAGAACAT GCTAAGCC.. ....ATCTCG CGCACAACAA AGCCCAGTGG
hspde_    1567 CTAAGTAATT GAAATGGCCC TAGCATTTTT TTCACCAATT AATTTACCTT


mpde_     1664 AAGAGCCT.G CTGTCCAATC AGCAC...AG ACGCA..... ...GGGGCAG
hspde_    1617 ACGTCTCTTG CACTTTAAAC AGAAGGGGAG ACACTCATTT TCTGGTTCAC

mpde_     1702 CG.......G CCAGGACCTG GCGG....GC CCCGC...AC CTGAGACCCT
hspde_    1667 TATTTGATAG CCATGGTATG TAGGCTGAGT CCCACTAAAT CTGAGGCCAT
```

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FIG. 4CONT'D

stop codon

```
mpde_    1738 GGAG.CAGAC AGAAGGTGCC ACGCCCTAAG GTAGCTGTC. .TGCTGA..T
hspde_   1717 TGTTTCATTT TCCTGGTG.. ..GCCCCAAG TTAGCTGCTA ATACTGTCTT

mpde_    1783 GCACGGCCA. .......TCT G.TCCGTCCA .....CAGGA GCACGGCC..
hspde_   1763 CCAAGGCCAC CATTAATTCT GATCTGTTTA ATGAACACGT GCAGAACCCA

mpde_    1817 ...ATCC... .........G TCC...GACT GC........ .CCTCGCAAC
hspde_   1813 AGAAACCTAG GTGAAAAGAG TACATAGATT GCTGTACCCT TCTTCAAGAC

mpde_    1840 AAGCCCATCA CGCTGGGTTT CGATGCCAT. .CCGCCTGCC A.CTTACC..
hspde_   1863 AAGCACATAA CTTGAGGTCA AGGACCAAGT GCTGTCTCCC AACTGAACAA

mpde_    1885 ...GCCTCCC TTCGTTGATC CAAGTGTACA AAAGCCATTG ...TCACCTC
hspde_   1913 GCAGTATACT CTGGGTTGTG GATTGATTCC TGGCCCTCTG ATTTGATCTC

mpde_    1929 AGCAT..... .TAGCTGCC. ..GAAATGGG CGGCTCTATC CCGTCATTGG
hspde_   1963 ATGCTGTTTC CTAGCACCCA GAGGAATGTG AAATTTGCAG GAGGAATTTC

mpde_    1970 AG..CTGAT. ...TCTGGGG CGGCTGCCCC AACCGAAAC. .........G
hspde_   2013 AGTTCTGATA AATTTTTACT CCCTGGAACT AAATAAAACC AGTTCTCGTG

mpde_    2004 CCTGGAAGTA AGAA..AGGG GTGCTTCTGC CGTGTTCGCC TCTGGCCCTT
hspde_   2063 CATGGAATAA AAACTTATGC CTCTTACTAG AATAATAAAT TGCAAAGATT

mpde_    2052 GGTCACGCTG ACTGGCAGTA GCTCCTAAGT CCAGAGCATT TTAACGTTTG
hspde_   2113 GAAAGAATTA AATGCAAAAA GAACTAAAAA CTAGAGCAAA AGATCAAGTG

mpde_    2102 CCATC..GGA CAGCTGACCT ...GCATGAC ACCAGCAT.. .ACTTGGAAC
hspde_   2163 AGAAGAAGAA AAGAGGAGGT AAGGAGAGAG ACAAGGAAGA AAGAAGGAGA

mpde_    2144 TGCAAAACTG GTCTTGCGTG CCAGAGCACA AACGAGAGTG TGAGAGAAA.
hspde_   2213 AGGAAAGGAA GAATAGTGAG G.ACAGGAAA GAAGAAAATG CAAGGGAAAT

mpde_    2193 ..GTACCTTC TATTT..TAA TAATAATTAT TATTATAAAA TA....ATAA
hspde_   2262 GGGAAAGGAC TCTGGGGTGA CCAGACTTCT CCTGGTCAGT ACCTGCATTC

mpde_    2235 ATCTTTTTAA CTTTT..ATA TTTCATGCAC CAGACAATGG GTCTAAAACT
hspde_   2312 ATCCTGTTTG TTACTCAATA TTTCTTTCCT AAAATATTCA TTTCACATCT

mpde_    2283 TTGGA...CA AGTAATACTC TGCGTACCCA AACCTAAGAG G......GGG
hspde_   2362 ATGGATTCCA ATGAAAAATA TATTTTTATG TGTCTTTGTG GAACACAGTG

mpde_    2324 TTC...ATTA TTTT.GCTAT T.GACTC... ..TATGCCAC ATTGGGTCCG
hspde_   2412 TTATAAATTG TTTTTGCCAG AAGAATAATT GTTATACAAT AATATATGTG

mpde_    2364 AGA..TGTGG CACCATTGCG ATTTCTGAAA CCACGCGTCC .CCTCCCATC
hspde_   2462 AAAACTTTAT TACAAAAGCC ATTATCATAA TCATTATTAT TCCTTCTATC

mpde_    2411 TGGTGGAAGG TGCTGTACAG CCCGTCCC.. ..TTTGCACC GTTAGCCAAT
hspde_   2512 ACA.GGTAAA TGCTTTAATG TCATTTTTCT GATTTTAAAA GTAGGGCAGG


mpde_    2457 CCGTCTTT.. ....TACGGA ...TTCAGTG ACCTGTTTAT ATTCACAA.G
hspde_   2561 TTAATTGTAG AAAGTAAGGA AAATTCAGGA AAGTGTTAGT TTGAACTATG

mpde_    2497 TGTACATTTT CTGT..AAAT ACCAAACGCT ACTGA..... ......TTCC
hspde_   2611 TGAAGTTGCT CTTTTTAAGG GCCAAAAACA GGAGACTTTT AGCACTTTCA

mpde_    2534 CATGC..CA. ....AAATAC ACGAGTATTA TGGGATTGCT A.....CCTG
hspde_   2661 TATGTTTCAG CTTGATATGA AAGAGAAAAC TGAAACTGCT AGTAATCCTG

mpde_    2571 .........T ATAAACAATG GCACTGTGAA CAGAATA... .CTGTTAGTT
hspde    2711 CCATCCAGGT ATAGTTCATG TTAACCTGGC TAGTTTATTT TCTTTTAGTC
```

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FIG. 4CONT'D

```
mpde_       2608 TTAATACAAG AGAATGCATT TGTAAATATG GTATAGAGTT TATTAATATA
hspde_      2761 TTTTTTCAAT ACAAA.CTTA TTTTAACAAA ATAT.GATTA TATTTGGGGA

mpde_       2658 CTGTTGTTCG CAGATAAAGG CCTTAACTTT AAAAAAAAAA AAAAAAAAA.
hspde_      2809 ACTTATTTTA CAGTTTACGT CCTGAAATTT TTTATTTACA ATAAAGACTT

mpde_       2708 .....:AAAA AAAAAAAAAA AAAAAGGGGC GGCCGCTCTA GAGGATCCCT
hspde_      2859 TTTTCCAAAT CAAAAAAAAA AAAAAAGGGC GGCCGCTCTA GAGGATCCCT

mpde_       2752 CGAGGGGCCC AAGCTTACGC GTGCATGCGA CGTCATAGCT CTCTCCCTAT
hspde_      2909 CGAGGGGCCC AAGCTTACGC GTGCATGCGA CGTCATAGCT CTCTCCCTAT

mpde_       2802 AGTGAGTCGT ATTATAAGCT AG..... .... 2823
hspde_      2959 AGTGAGTCGT ATTATAAGCT AGGCACTGGC CGTC 2992
```

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FIG. 5

Protien Alignment of the Murine & Human PDE_XIV

```
CLUSTAL W (1.7) multiple sequence alignment

mpde            MSCLMVERCGEVLFESPEQSVKCVCMLGDVRLRGQTGVPAERRGSYPFIDFRLLNNTTHS 60
hspde           MSCLMVERCGEILFENPDQNAKCVCMLGDIRLRGQTGVRAERRGSYPFIDFRLLNSTTYS 60
                ***********:***.*:*. .********:******** ***************.**:*

mpde            GEIGTKKKVKRLLSFQRYFHASRLLRGIIPQAPLHLLDEDYLGQARHMLSKVGTWDFDIF 120
hspde           GEIGTKKKVKRLLSFQRYFHASRLLRGIIPQAPLHLLDEDYLGQARHMLSKVGMWDFDIF 120
                ************************************************** ******

mpde            LFDRLTNGNSLVTLLCHLFNSHGLIHHFKLDMVTLHRFLVMVQEDYHGHNPYHNAVHAAD 180
hspde           LFDRLTNGNSLVTLLCHLFNTHGLIHHFKLDMVTLHRFLVMVQEDYHSQNPYHNAVHAAD 180
                ********************:************************.:************

mpde            VTQAMHCYLKEPKLASFLTPLDIMLGLLAAAAHDVDHPGVNQPFLIKTNHHLANLYQNMS 240
hspde           VTQAMHCYLKEPKLASFLTPLDIMLGLLAAAAHDVDHPGVNQPFLIKTNHHLANLYQNMS 240
                ************************************************************

mpde            VLENHHWRSTIGMLRESRLLAHLPKEMTQDIEQQLGSLILATDINRQNEFLTRLKAHLHN 300
hspde           VLENHHWRSTIGMLRESRLLAHLPKEMT---------------------------------- 268
                ******************************

mpde            KDLRLENVQDRHFMLQIALKCADICNPCRIWEMSKQWSERVCEEFYRQGDLEQKFELEIS 360
hspde           ------------------------------------------------------------

mpde            PLCNQQKDSIPSIQIGFMTYIVEPLFREWARFTGNSTLSENMLSHLAHNKAQWKSLLSNQ 420
hspde           ------------------------------------------------------------


mpde            HRRRGSGQDLAGPAPETLEQTEGATP 446
hspde           --------------------------
```

Zinc binding motif's are highlighted in bold.
Non-Catalytic domain in italics.

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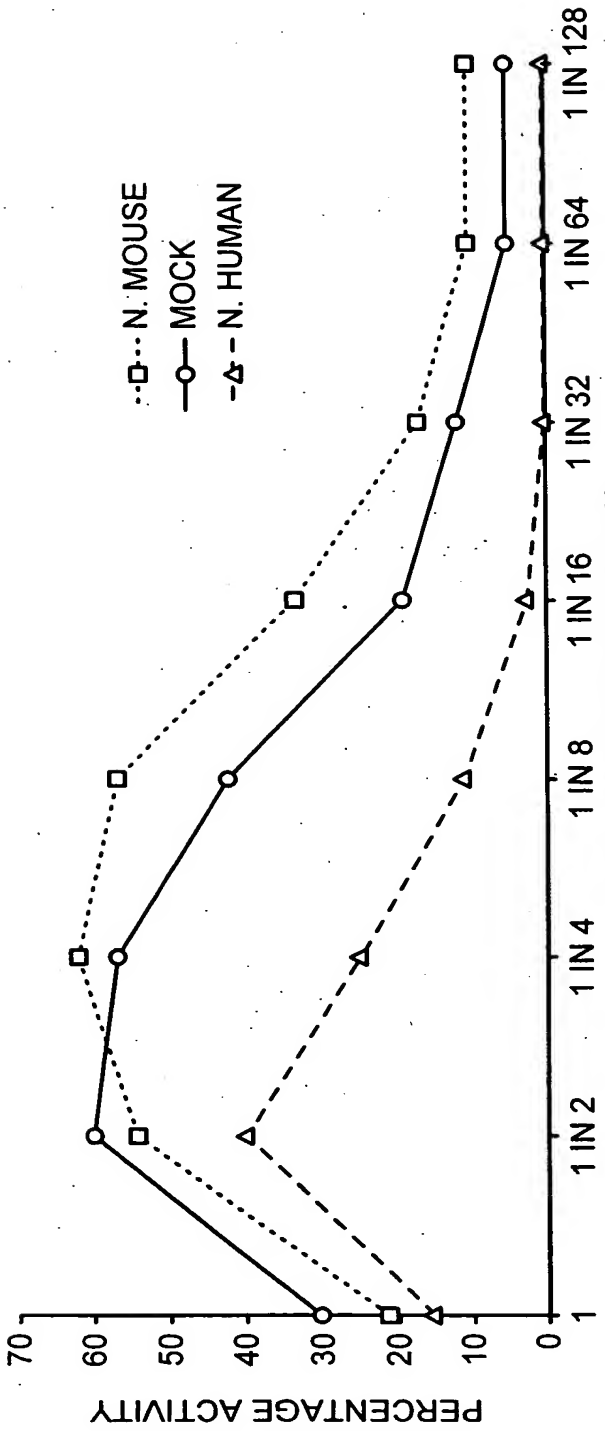

FIG. 6

SPA ASSAY TO DETERMINE THE cAMP HYDROLYTIC ACTIVITY OF MURINE AND HUMAN PDE_XIV